In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 22, 2024

CAROL WILKINSON,	*	PUBLISHED
Petitioner,	*	No. 18-1829V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Influenza ("Flu") Vaccine; Polymyalgia Rheumatica ("PMR").
Respondent.	*	

Verne E. Paradie, Jr., Paradie, Rabasco & Seasonwein, Lewiston, ME, for Petitioner.
Madylan Louise Yarc, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION[1]

I. INTRODUCTION

On November 29, 2018, Carol Wilkinson ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2018).[2] Petitioner alleges that she suffered polymyalgia rheumatica ("PMR") as a result of an influenza ("flu") vaccination she received on December 1, 2015.

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

2016. Petition at Preamble (ECF No. 1).[3] Respondent argues against compensation, stating that "this case is not appropriate for compensation under the [Vaccine] Act." Respondent's Report ("Resp. Rept.") at 1-2 (ECF No. 51).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that Petitioner has failed to provide preponderant evidence that her flu vaccination caused her PMR and thus, she has not satisfied her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, the petition must be dismissed.

II. ISSUES TO BE DECIDED

Diagnosis is not at issue. Joint Pre-Hearing Submission, filed May 26, 2022, at 1 (ECF No. 77). The only disputed fact is the onset of Petitioner's PMR symptoms. Id. Causation is also in dispute. Id. At issue is whether Petitioner has provided preponderant evidence of causation for all three Althen prongs. Id.

III. BACKGROUND

A. Medical Terminology

"Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease affecting people older than 50 years and is [two to three] times more common in women." Petitioner's Exhibit ("Pet. Ex.") 29 at 1.[4] Common symptoms include "pain and morning stiffness in the shoulder and pelvic girdle." Id. Fatigue, fever, and weight loss may also be present. Id. "The pathology includes synovial[5] and periarticular[6] inflammation and muscular

[3] Petitioner filed two amended petitions throughout the course of litigation. Neither change the substance of the claim. Amended ("Am.") Petition, filed Aug. 14, 2019 (ECF No. 16); Am. Petition, filed Apr. 23, 2020 (ECF No. 39).

[4] Ingrid E. Lundberg, An Update on Polymyalgia Rheumatica, 292 J. Internal Med. 717 (2022).

[5] The synovium is the "synovial membrane of articular capsule: the inner of the two layers of the articular capsule of a synovial joint, composed of loose connective tissue and having a free smooth surface that lines the joint cavity. It secretes the synovial fluid." Membrana Synovialis Capsulae Articularis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition? id=88558 (last visited July 17, 2024); see also Synovial, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=48564 (last visited July 17, 2024).

[6] Periarticular means "around a joint." Periarticular, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=37717 (last visited July 17, 2024).

vasculopathy."[7] Id. Diagnosis is made based on clinical history and the presence of elevated inflammatory markers. Id. Glucocorticoids (prednisolone) are the mainstay of therapy, with biologics used to decrease the toxicity of steroids. Id.

PMR is sometimes associated with giant cell arteritis ("GCA"), a systemic vasculitis that "may involve several large vessels, often but not always including the temporal artery." Pet. Ex. 29 at 4. Symptoms of vasculitis include headache, visual symptoms, fever, weight loss, and fatigue. Id.

B. Procedural History

Petitioner filed her petition in November 2018 and supporting medical records in December 2018.[8] Petition; Pet. Exs. 1-10. Respondent filed his Rule 4(c) report on December 4, 2019. Resp. Rept.

On March 25, 2020, Petitioner filed an expert report from Dr. Petros Efthimiou. Pet. Ex. 17. On June 9, 2020, Respondent filed an expert report from Dr. Christopher A. Mecoli. Resp. Ex. A.

The undersigned held a Rule 5 conference on August 26, 2020. Rule 5 Order dated Aug. 26, 2020 (ECF No. 54). The undersigned preliminarily found diagnosis was not in dispute and that there was a temporal association. Id. at 1-2. Additional expert reports on Althen prong one were recommended. Id. at 2. Petitioner filed a supplemental expert report from Dr. Efthimiou on November 10, 2020. Pet. Ex. 22. Respondent filed a supplemental expert report from Dr. Mecoli on February 1, 2021. Resp. Ex. C.

An entitlement hearing was initially scheduled for June 2022. Order dated Jan. 21, 2021 (ECF No. 64). The parties filed pre-hearing submissions. Pet. Pre-Hearing Submission, filed Apr. 23, 2022 (ECF No. 71); Resp. Pre-Hearing Submission, filed May 25, 2022 (ECF No. 74). The entitlement hearing was ultimately rescheduled for, and held on, November 15, 2023. See Order dated Jan. 21, 2021 (ECF No. 64); Order dated June 13, 2022 (ECF No. 78); Order dated July 18, 2022 (ECF No. 82); Order dated Oct. 4, 2022 (ECF No. 89); Order dated Nov. 15, 2023 (ECF No. 109). Prior to the hearing, Petitioner elected to file an updated pre-hearing submission. Pet. Updated Pre-Hearing Submission, filed Oct. 15, 2023 (ECF No. 102). Following the hearing, the parties waived filing post-hearing briefs. Pet. Status Rept., filed Nov. 18, 2023 (ECF No. 111).

This matter is now ripe for adjudication.

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[7] Vasculopathy is "any disorder of the blood vessels." Vasculopathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=52622 (last visited July 17, 2024).

[8] Petitioner continued to file medical records throughout the course of litigation.

C. Factual History

1. Medical History[9]

At the time of her flu vaccination in December 2015, Petitioner had a history of migraine headaches, gastroesophageal reflux disease, hyperlipidemia, depression, anxiety, hypothyroidism, irritable bowel syndrome, cervical osteoarthritis, kidney stones, osteopenia, and hoarseness due to vocal cord paralysis. Pet. Ex. 2 at 78-79. She was taking several medications for these conditions. Id. at 78.

On December 1, 2015, at 74 years old, Petitioner saw her primary care physician ("PCP") for follow-up of her blood pressure. Pet. Ex. 2 at 70. She had been seen at an urgent care on November 19, 2015 for a urinary tract infection when elevated blood pressure was noted. Id. Her blood pressure remained elevated at this visit. Id. She received a high dose flu vaccination. Id. at 73.

Petitioner called her PCP, Dr. Wendy Cathcart, on December 28, 2015, complaining of right-hand pain, swelling, and weakness that "came on gradually over the last week." Pet. Ex. 2 at 67. Petitioner reported "warmth where there [was] swelling," but denied numbness and tingling. Id. Petitioner also reported left hip pain that "started in the left and then spread to the right a few weeks before." Id. Petitioner thought the pain could be related to her simvastatin medication, so she stopped taking it, but her hip pain and "pain going down the back of her legs" did not improve. Id. Petitioner related that her hip pain began about one week after she received a flu vaccination. Id.

Dr. Cathcart saw Petitioner that day and noted "significant" right hand swelling with redness and tenderness in the proximal interphalangeal ("PIP") and metacarpophalangeal ("MCP") joints. Pet. Ex. 2 at 68. Her left hand was unaffected. Id. Dr. Cathcart documented "slightly" decreased range of motion with pain on internal rotation in both hips. Id. Dr. Cathcart assessed Petitioner with inflammatory arthritis with differential diagnoses including reactive arthritis, rheumatoid arthritis, pseudogout, and gout. Id. Dr. Cathcart prescribed an eight-day prednisone taper, ordered several lab tests, and referred Petitioner to a rheumatologist. Id. at 68-69. A right-hand X-ray was unremarkable. Pet. Ex. 12 at 23.

Petitioner saw rheumatologist Dr. Brian Keroack on December 28, 2015, on referral from Dr. Cathcart, for severe right-hand pain. Pet. Ex. 1 at 22. Dr. Keroack noted that Petitioner had "significant myalgias of her thighs and later her shoulders," starting about one week after a flu vaccination. Id. He further noted that her symptoms had persisted and she experienced over one hour of stiffness in the morning. Id. In the prior few days, she developed significant pain and discomfort in her right hand and was referred for evaluation. Id. On examination, she had difficulty raising her arms, pain on transferring from the chair, and significant tenderness of the

[9] Petitioner's medical history is taken from Respondent's pre-hearing submission which has been edited by the undersigned. See Resp. Pre-Hearing Submission at 2-9. For more current records related to Petitioner's PMR, see Pet. Ex. 26. The updated records have not been summarized here, as they are not relevant to the issues of onset or causation.

third flexor tendon in the right hand. Id. Her sedimentation rate ("ESR") and C-reactive protein ("CRP") levels were elevated. Id. An ultrasound of the right hand and wrist showed no evidence of synovitis of the third MCP or PIP joints or the wrist. Id. There was "extensive tenosynovitis[10] with positive power Doppler signal in the [third] flexor tendon." Id. Dr. Keroack diagnosed Petitioner with PMR "with associated inflammatory tenosynovitis," administered a steroid injection in Petitioner's right third flexor tendon, and placed her on prednisone 15 mg daily. Id. at 22-23.

Petitioner returned to Dr. Keroack for follow-up on January 11, 2016. Pet. Ex. 1 at 18. Her cyclic citrullinated peptide ("CCP")[11] and rheumatoid factor ("RF")[12] tests were negative. Id. at 19. She reported improvement the following morning after taking 10 mg of prednisone, which Dr. Keroack indicated was consistent with PMR. Id. He noted "[i]t took a couple of days for the tenosynovitis to clear up, but she [was] really back to herself." Id. Dr. Keroack further noted that Petitioner was "really functioning at a very high level." Id. at 18. She was able to transfer easily and had normal range of motion of all peripheral and central joints. Id. He noted that she was not having any issues with a 10 mg dose of prednisone, but he recommended that she begin a slow taper, decreasing her dosage by 1 mg every two weeks until she was down to 7 mg per day. Id. at 19. He planned to see her in follow-up two months later. Id.

A handwritten note in Dr. Keroack's records dated January 26, 2016 documented that Petitioner's "middle finger [was] swollen in [morning]," but that when she took prednisone, her finger was "ok." Pet. Ex. 1 at 18. The notes contained a list of symptoms including fatigue, "winded," "glands [were] swollen," and "sometimes [got] [shortness of breath]." Id. The note further indicated that an unidentified person spoke with Dr. Keroack and he wanted Petitioner to change Petitioner's dosage of prednisone to 5 mg twice per day. Id.

On February 16, 2016, Petitioner returned to Dr. Keroack for follow-up, at which time her PMR was considered in remission. Pet. Ex. 1 at 17. Dr. Keroack planned to further taper Petitioner's prednisone dose down to 7 mg. Id. On April 19, 2016, Petitioner reported that her right third finger became swollen when she decreased her dosage from 9 mg to 8 mg. Id. After adjusting her dosage, she stated that her symptoms were "livable." Id. at 15. Since Petitioner

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[10] Tenosynovitis is the "inflammation of a tendon sheath." Tenosynovitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=49214 (last visited July 17, 2024).

[11] CCP is "a synthetic, citrulline-containing peptide with a cyclic structure, used in assays for rheumatoid arthritis; the presence of antibodies to this peptide is highly specific for rheumatoid arthritis." Cyclic Citrullinated Peptide, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=97140 (last visited July 17, 2024).

[12] RF refers to "antibodies directed against antigenic determinants . . . in the Fc region of the IgG class of immunoglobulins; these are found in the serum of about 80 percent of persons with classical or definite rheumatoid arthritis." Rheumatoid Factor, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=74591 (last visited July 17, 2024).

did not have myalgias in her shoulders and hips, Dr. Keroack stated her PMR symptoms were "quiet." Id. He noted that there was "definite synovial thickening of the [third] MCP, [third] PIP as well as tenosynovial thickening in that [third] finger as well." Id. He further documented that her other joints were unremarkable. Id. Dr. Keroack questioned whether Petitioner was suffering from seronegative rheumatoid arthritis versus PMR. Id. Her CCP and RF levels were negative, but she was "showing some signs of recurrent synovitis of the [third] finger." Id. He planned to continue tapering Petitioner's prednisone dosage and, if she had a flare of her finger synovitis, he planned to use Plaquenil[13] as a long-term treatment for potential seronegative rheumatoid arthritis. Id.

On May 23, 2016, Petitioner called her PCP reporting shortness of breath and that she did not feel well. Pet. Ex. 2 at 59. She reported that Dr. Keroack thought her symptoms were related to prednisone usage. Id. Petitioner requested Tramadol to treat neck pain. Id. Dr. Cathcart noted that her screening labs were unremarkable except for elevated calcium, which she suspected was the cause of Petitioner's fatigue and was related to the prednisone tapering. Id. at 62.

A handwritten note from June 23, 2016 documented a phone call from Petitioner to Dr. Keroack's office for complaints of swelling that was "so bad [that] she hurts when she walks." Pet. Ex. 1 at 15. Petitioner was taking prednisone 10 mg daily. Id. Dr. Keroack recommended that Petitioner see her PCP for a diuretic. Id. Petitioner saw Dr. Keroack on July 5, 2016 for ankle swelling that she thought was related to her inflammatory arthritis. Id. at 10. She also complained that she bruised easily and had facial puffiness. Id. Dr. Keroack noted that the swelling was pitting edema, not arthritis, and that her symptoms were related to chronic steroid usage. Id. In a letter to Dr. Cathcart, Dr. Keroack related that Petitioner had increased her prednisone dosage due to edema in her lower extremities, but that her edema was likely related to her prednisone usage rather than due to inflammatory arthritis. Id. at 12. He noted that Petitioner was asymptomatic with respect to her "PMR-type signs and symptoms and from the inflammatory tenosynovitis" and he recommended a strict tapering regimen. Id.

On July 13, 2016, Petitioner underwent an endocrine surgery consultation with Drs. Scha'chia Murphy and Dougald C. MacGillivray for her symptomatic hyperparathyroidism. Pet. Ex. 9 at 7. Petitioner reported symptoms of fatigue, weight gain, swelling, depression, dry skin, and concentration difficulties that she attributed to taking prednisone for PMR. Id. She had elevated calcium and thyroid hormone levels. Id. An ultrasound conducted in the office showed a large left parathyroid gland; a biopsy of a right thyroid nodule was performed. Id. at 12. Drs. Murphy and MacGillivray diagnosed Petitioner with probable enlarged left parathyroid gland

[13] Plaquenil is trademark for of hydroxychloroquine sulfate which is "a 4-aminoquinoline compound with antiprotozoal and antiinflammatory properties, used for suppression and treatment of malaria, for suppression of lupus erythematosus, and as an antiinflammatory disease-modifying antirheumatic drug in treatment of rheumatoid arthritis." Plaquenil, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39441 (last visited July 17, 2024); Hydroxychloroquine Sulfate, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=23495 (last visited July 17, 2024).

and advised Petitioner that her "symptoms of hyperparathyroidism may overlap with her [PMR] and steroid symptoms." Id. After discussing management options, Petitioner agreed to undergo a minimally invasive parathyroidectomy. Id.

The surgery to remove Petitioner's left inferior parathyroid gland took place on August 1, 2016. Pet. Ex. 9 at 5-6. On August 17, 2016, Petitioner returned to see Dr. Keroack for follow-up of her PMR. Pet. Ex. 1 at 9. Dr. Keroack noted Petitioner's recent thyroid surgery that found a benign tumor. Id. Petitioner was taking 5 mg of prednisone and was "really functioning at a very high level other than her right [third] finger," which was "puffy" but painless. Id. Further tapering of her prednisone was planned. Id. At an August 24, 2016 post-operative visit with her surgeon's office, Petitioner reported feeling well and that she was taking her calcium supplement. Pet. Ex. 9 at 1-4. On September 28, 2016, at a visit with Dr. Daniel Oppenheim for thyroid surgery follow-up, Petitioner reported improved energy since her surgery, but continued to have difficulty breathing, which she attributed to prednisone use. Pet. Ex. 7 at 1. She also continued to have intermittent problems with swallowing and thinning hair. Id. Dr. Oppenheim assessed Petitioner as clinically stable after "curative parathyroidectomy." Id. Dr. Oppenheim recommended a trial of decreased prednisone. Id. No further endocrine follow-up was needed. Id.

On September 23, 2016, Petitioner saw Dr. Cathcart for ankle swelling. Pet. Ex. 2 at 38. She complained of a flare of her PMR and had spoken with Dr. Keroack who had increased her prednisone to 7 mg daily. Id. Although she complained of difficulty taking a deep breath, Petitioner localized her pain to her epigastric area rather than her chest. Id. Petitioner's husband noted that she was suffering from heightened anxiety and questioned whether her shortness of breath was related. Id. Dr. Cathcart ordered a chest X-ray and computed tomography ("CT") scan of the abdomen. Id. at 40. An October 6, 2016 ultrasound and CT scan showed extensive deep vein thrombosis ("DVT") and Petitioner was started on long-term anticoagulation therapy. Pet. Ex. 12 at 31-37.

At a follow-up visit with Dr. Cathcart on October 19, 2016,[14] Petitioner reported that since starting anticoagulation therapy, her dyspnea, tachycardia, and diaphragm pain related to her pulmonary embolism had decreased. Pet. Ex. 2 at 27. She had some mild exertional dyspnea that was likely related to weight gain since starting prednisone and mild swelling of her left lower extremity above the ankle that was better in the morning and worse at the end of the day, but no leg pain. Id. Dr. Cathcart ordered continued anticoagulation therapy, exercise, continued prednisone therapy at 5 mg once a day, and continued treatment with sertraline for anxiety. Id. at 29.

On November 10, 2016, Petitioner saw Dr. Cathcart for bilateral leg pain. Pet. Ex. 2 at 23. She was on Coumadin for DVT in her left leg and on chronic prednisone for her PMR. Id. Her current prednisone dose was 7 mg daily. Id. She had minimal pain in her ankles and worse

[14] It appears that flu and zoster vaccines were planned at this visit. See Pet. Ex. 2 at 27 (noting "AdvDir, Flu, Zost" under the second "Reason for Appointment"). A similar note was included in in Petitioner's September 23, 2016 visit. See id. at 38. It is unclear if the vaccines were administered during either of these visits.

swelling at the end of the day. Id. Petitioner also reported a searing pain in her legs at night that was worse in the left leg and the return of migraine headaches up to two times per week. Id. Dr. Cathcart diagnosed Petitioner's leg pain as likely steroid myopathy "as it [was] more distal and not PMR." Id. at 25. She ordered labs and planned to decrease Petitioner's prednisone dosage if her lab results were normal. Id. Petitioner was to continue taking Synthroid and Coumadin. Id. Dr. Cathcart noted that Petitioner's headaches may be related to high blood pressure and recommended that she resume checking her pressure at home and to contact her office for medication if her readings were consistently high. Id.

On March 10, 2017, Petitioner returned for follow-up with Dr. Keroack and reported experiencing significant, increasing discomfort in her shoulders and legs when her prednisone dose was tapered down to 5 mg. Pet. Ex. 1 at 6. She increased her dosage to 8 mg over the prior few weeks and had a dramatic improvement in her symptoms. Id. Dr. Keroack planned to start tapering Petitioner's prednisone dosage after four or five weeks, but, if she failed this effort, he planned to use either Plaquenil or methotrexate as a steroid-sparing agent. Id. In May 2017, Petitioner was down to 6 mg of prednisone and reported feeling well with few aches and pains. Id. at 4. She had no "PMR-type signs or symptoms." Id.

In July 2017, at a follow-up visit, Dr. Cathcart noted that Petitioner had a flare of her PMR whenever her prednisone dose was tapered down to 5 mg. Pet. Ex. 2 at 16. She had recently tried to taper her dosage again and had increased symptoms in her hands. Id. After increasing her dosage to 7 mg, her symptoms had "calmed down." Id. She had dyspnea at the higher dose, had developed cushingoid features, and her headaches increased in frequency. Id. Petitioner had completed six months of Coumadin therapy in April and had not had any left leg swelling since. Id. She reported occasional swelling in her right ankle that she attributed to PMR. Id. Testing showed "very elevated" thyroid hormones that Dr. Cathcart explained could be the source of some of Petitioner's joint pain. Id. On examination, Petitioner had swelling in her right ankle and MCP and PIP joints bilaterally. Id. at 19. She had normal range of motion in her upper and lower extremity joints and in the left hip. Id. Muscular strength and reflexes were normal. Id. Dr. Cathcart recommended that Petitioner continue her current medications, including prednisone (5 mg per day), migraine medication (Imitrex), and Synthroid. Id. at 20.

On September 18, 2017, Dr. Keroack noted that Petitioner was "all in all functioning at a very high level" without any PMR pain. Pet. Ex. 1 at 2. She was stable on 5 mg of prednisone. Id. He planned to decrease her dosage by 1 mg per month. Id. Between October 2017 and March 2018, Petitioner's prednisone dosage varied between 5 and 7 mg. See, e.g., id. at 1; Pet. Ex. 2 at 7. On March 20, 2018, Petitioner saw rheumatologist Dr. Marc Miller at Dr. Keroack's office. Pet. Ex. 1 at 1. Dr. Miller noted that Petitioner may be describing steroid withdrawal versus true increased PMR activity. Id.

Petitioner filed updated records showing that she continues to see Dr. Keroack for treatment of her PMR. See generally Pet. Exs. 24, 26.

2. Petitioner's Testimony

At the time of the hearing, November 15, 2013, Petitioner was 82 years of age (she was 74 when she received the vaccination at issue) and retired from employment. Transcript ("Tr.") 7, 12. Prior to retirement, she was a real estate broker. Tr. 7. She had also previously been employed as a legal secretary and assistant tour coordinator. Id. Her pre-vaccination history was significant for migraine headaches, gastroesophageal reflux disease, hyperlipidemia, depression, anxiety, irritable bowel syndrome, and cervical osteoarthritis. Tr. 38-39.

Before her flu vaccination in 2015, Petitioner had received prior flu vaccinations.[15] Tr. 8. She testified that she had an adverse reaction to a flu vaccination in 2011; she lost her voice for approximately six months. Id. She received speech therapy in order to regain the ability to talk. Tr. 35. None of Petitioner's health care providers in 2011 attributed her inability to talk to her flu vaccination. Tr. 36. She received flu vaccinations after that event in 2013 and 2014. Id. After the 2015 flu vaccine, the vaccine at issue here, she has received one flu vaccination without any adverse reaction. Tr. 8.

About eight to 10 days after receiving her flu vaccination in 2015, Petitioner began to feel achy from her shoulders down to her elbows. Tr. 14. She could hardly lift her arms, but since it was Christmas time, she took pain pills and "went through it." Id. Three days after Christmas, the fingers in her right hand curled up, so she saw her physician, Dr. Cathcart, who referred her to a rheumatologist, Dr. Keroack, who told her that she had PMR. Tr. 14, 17. Dr. Keroack prescribed prednisone, and she had an injection in her right hand. Tr. 20. Although prednisone improved Petitioner's symptoms, when she attempted to reduce her doses, she would have worsening symptoms or flare-ups of her PMR. Tr. 22-24. The prednisone also caused Petitioner to have swelling in her feet and legs. Id. In addition to prednisone, Petitioner also took Plaquenil for a while. Tr. 27.

Petitioner continues to see Dr. Keroack for her PMR. Tr. 28. And she continues to try to wean off prednisone, but when she quits taking it, all the symptoms return. Id. At the time of the hearing, Petitioner was taking Prednisone 10 mg and Plaquenil 200 mgs twice a day. Id.

Prior to the onset of her PMR, Petitioner testified she was generally healthy. Tr. 32. Her husband was alive, and he also had PMR, with similar symptoms, and he saw Dr. Keroack as well. Tr. 33. Petitioner testified that her husband also developed PMR after receiving a flu shot in 2011. Tr. 40.

[15] For a record of Petitioner's vaccinations, see Pet. Ex. 6.

D. Expert Reports

1. Petitioner's Expert, Dr. Petros Efthimiou[16]

a. Background and Qualifications

Dr. Efthimiou is board certified in internal medicine and rheumatology. Pet. Ex. 17 at 1; Tr. 44. He received his M.D. from the University of Ioannina Medical School in Ioannina, Greece. Pet. Ex. 30 at 1. Thereafter, he completed an internal medicine residency at Brown University/Rhode Island Hospital and a rheumatology fellowship at the Hospital for Special Surgery/Weill Cornell Medical Center. Id.; Tr. 44. Dr. Efthimiou is currently an attending rheumatologist at White Plains Hospital and a clinical professor at Albert Einstein College of Medicine in New York. Tr. 43. His clinical practice consists of diagnosing and treating musculoskeletal, autoimmune, and autoinflammatory conditions, including rheumatoid arthritis, PMR, GCA, and other vasculitides. Tr. 46. He has conducted research on inflammatory rheumatic conditions such as PMR, inflammatory arthritis, and tenosynovitis. Pet. Ex. 17 at 2; Tr. 47. Dr. Efthimiou has authored or co-authored numerous academic papers as well as a rheumatology textbook chapter. Pet. Ex. 17 at 2; Pet. Ex. 30 at 10-21.

b. Opinion

Dr. Efthimiou agreed with Petitioner's diagnosis of PMR. Tr. 60. He also opined that Petitioner had tenosynovitis, which he described as "inflammation of the tendons and the synovium, [] or lining of the joint," characteristically seen in PMR. Id. He testified that PMR is an autoimmune condition. Id.

i. Althen Prong One

Dr. Efthimiou offered several opinions about the mechanism of causation. In his first expert report, Dr. Efthimiou stated that "[t]he vaccination le[d] to an aberrant activation of the immune system and the clinical manifestations of [PMR]." Pet. Ex. 17 at 3. He did not explain what he meant by "an aberrant activation" or otherwise describe this theory or how it could cause PMR.

In his second expert report, he wrote "[i]t is the scope of the vaccination to activate the immune system and elicit an immune response, specific for the antigens associated with the flu viruses that were selected for that particular season." Pet. Ex. 22 at 2. He explained that because the antigens in the flu vaccine change from year to year, "the antigenic challenge presented to the individual differs considerably." Id. Although he did not offer a general theory of causation about how the flu vaccine can cause PMR, he opined that Petitioner's "genetic constitution" and "immune system response to the particular antigenic mix that she was challenged with in December 2015, le[d] to a broad, non-specific, overactivation of her immune system." Id. He did not explain what he meant by this statement, or how the flu vaccine could lead to a non-specific immune system activation that could cause PMR.

[16] Dr. Efthimiou submitted two expert reports and testified at the hearing. Pet. Exs. 17, 22; Tr. 3.

At the hearing, Dr. Efthimiou agreed that the exact mechanism of causation is not understood. Tr. 61. He opined that the cause of PMR is "a break in [] immune tolerance, and the immune system starts attacking the joint, the tendons, the synovium, [and] the lining of the cell." Id. He also testified that inflammatory cytokines play a role in triggering inflammation. Id. Then he pivoted from his statement of cytokines to opine that the flu vaccine can cause PMR through the mechanism of molecular mimicry.[17] Tr. 62-63, 65. He testified that there can be a "mild overlap" of antigens in the vaccine with antigens in the body, and the immune system views the tissues in the body as "potential enemies . . . and then starts attacking them." Tr. 63. According to Dr. Efthimiou, this results in an "increase of proinflammatory cytokines," including interleukin 6 (IL-6), "a major proinflammatory cytokine[] [] involved in this pathogenesis." Tr. 62. Cytokines circulate in the blood and tissues and cause inflammation, which causes pain, swelling, and morning stiffness, which are characteristic of PMR. Tr. 64.

He then stated that some cytokines are pro-inflammatory (such as IL-6 and tumor necrosis factor alpha), and others are anti-inflammatory (interleukin 10 or interleukin 1 receptor antagonist). Tr. 66. An imbalance between the pro- and anti-inflammatory cytokines can cause systemic inflammation. Id. And he explained that cytokines are not typically tested for because commercial tests for them are not available. Tr. 67. Instead, other indices of inflammation, such as ESR and CRP, are tested. Id. While these tests are not diagnostic of PMR, they aid in evaluating the presence of inflammation. Tr. 68-69.

On cross-examination, Dr. Efthimiou agreed that that the pathogenesis of PMR is not clear, and the cause is multifactorial or unknown. Tr. 80. The medical literature suggests that genetic factors may play a role in causation and that PMR may be a paraneoplastic phenomenon. Tr. 82. He also agreed that PMR predominately affects woman over the age of 50. Id.

In support of his opinions, Dr. Efthimiou cited medical articles. The first, by Iwata and Mizuno,[18] was a case report of an 85-year-old who developed PMR after a flu B infection. Pet. Ex. 18 at 1. The patient did not receive a flu vaccination. Id. The authors acknowledged that the cause of PMR "remains unknown," although various infectious agents have been suggested as casual. Id. at 2. They also stated that "[t]he exact role of [flu] vaccination on the development of PMR remains unknown." Id.

[17] Molecular mimicry is "a model of autoimmunity in which an immune response to a foreign antigen containing a peptide region that mimics a self epitope provokes cross-reactivity to a self protein." Molecular Mimicry, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=89392 (last visited July 17, 2024).

[18] Kentaro Iwata & Yasushi Mizuno, A Case of Polymyalgia Rheumatica Following Influenza B Infection, 8 Int'l J. Gen. Med. 345 (2015).

The second paper, by Bassendine and Bridge,[19] reported a case involving a severe flare of PMR in a 70-year-old after receipt of an adjuvanted trivalent flu vaccination. Pet. Ex. 19 at 1. The authors stated "[t]he etiology and pathogenesis of PMR remain obscure." Id. They questioned the role of the adjuvant in triggering the PMR flare. Id. at 3. When questioned about the Bessendine and Bridge case report, Dr. Efthimiou agreed the flu vaccine in that case contained an adjuvant, whereas Petitioner's vaccination did not contain an adjuvant. Tr. 87.

Several papers referenced by Dr. Efthimiou addressed case reports of patients with combined PMR and GCA. Soriano et al.[20] discussed several possible mechanisms, including a possible genetic association (HLA typing[21] was done in two patients) which could be a genetic predisposing factor. Pet. Ex. 20 at 3; see also Pet. Ex. 29 at 2 (discussing the gene variant HLA-DR4 that is present in cases where PMR and GCA occur together); Pet. Ex. 23 at 1 (reporting on a 70-year-old woman who developed GCA and PMR following the flu vaccine).[22] Dr. Efthimiou agreed that the Wada et al. case report dealt with PMR and GCA, and Petitioner did not have GCA. Tr. 87-89.

Regarding his proposed theory of molecular mimicry, Dr. Efthimiou agreed that the antigen or component of the vaccine which allegedly causes PMR is not known. Tr. 90-92. And when asked about molecular mimicry, Dr. Efthimiou responded by testifying about the innate immune system and its contribution to autoinflammatory conditions via cytokine driven processes. Tr. 92-93.

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[19] Margaret F. Bassendine & Simon H. Bridge, Relapse of Polymyalgia Rheumatica Following Adjuvanted Influenza Vaccine: A Case-Based Review, 7 Eur. J. Rheumatology 37 (2020).

[20] A. Soriano et al., Giant Cell Arteritis and Polymyalgia Rheumatica After Influenza Vaccination: Report of 10 Cases and Review of the Literature, 21 Lupus 153 (2012).

[21] HLA typing is the "determination of the human leukocyte antigens (HLA) possessed by an individual. Class I antigens (HLA-A, -B, and -C) are detected by lymphocyte microcytotoxicity assay using standard typing sera. Class II antigens are detected by one-way mixed lymphocyte cultures using panels of homozygous typing cells" or by primed lymphocyte typing. HLA Typing, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=116068 (last visited July 17, 2024). "DR Class II antigens are also detected by lymphocyte microtoxicity assay using B lymphocytes and anti-DR antibody types. HLA typing is used to identify compatible donors and recipients for transplantation or platelet or granulocyte transfusion, to establish associations of human leukocyte antigens with diseases, and in paternity testing." Id. Specifically in the Soriano et al. article, HLA typing revealed "the presence of alleles at the DRB1 locus." Pet. Ex. 20 at 2. Petitioner did not have GCA, and she did not have HLA typing done.

[22] Makoto Wada et al., Giant Cell Arteritis with Polymyalgia Rheumatica Associated with Influenza Vaccination, 38 J. Dermatology 1099 (2011).

Regarding the high dose flu vaccine administered to Petitioner, Dr. Efthimiou testified that it contained about four times the ingredients of the regular flu vaccine. Tr. 97-98. He agreed this increased dose is needed due to immunosenescence[23] in the older population, who cannot achieve a protective immunological response without a stronger vaccine. Tr. 98.

ii. Althen Prongs Two and Three

Dr. Efthimiou opined, to a reasonable degree of medical certainty, that Petitioner's PMR and inflammatory tenosynovitis were triggered by the flu vaccine she received in 2015. Pet. Ex. 17 at 4. In his second expert report, Dr. Efthimiou characterized Petitioner's response as a "broad, non-specific, over-activation of her immune system. The interplay of her own genetic constitution with the particular antigenic challenge" of her vaccination, "lead to the clinical manifestations autoimmunity, such as [] PMR and tenosynovitis." Pet. Ex. 22 at 2. According to Dr. Efthimiou, Petitioner had "quite an inflammatory response." Id. at 76. He opined that vaccination is a "distinct event known in the literature to possibly, in rare occasions, elicit such a response." Tr. 78. He concluded that Petitioner's clinical course was consistent with vaccination as the trigger of her PMR. Id.

Dr. Efthimiou acknowledged that Petitioner did not have any adverse effects of the prior dose of the high dose flu vaccine she received in 2014. Tr. 83.

He further opined that there were no other causes noted in the Petitioner's history associated with the presentation of her PMR. Tr. 83. Dr. Efthimiou concluded that Petitioner's presentation, course, and supporting data suggests that it was the vaccination that triggered the presentation of PMR. Tr. 79.

Regarding onset, Dr. Efthimiou opined that Petitioner's symptoms PMR began about eight to 10 days after vaccination, which was an appropriate time frame. Tr. 77. Based on the literature, he testified that anywhere between one day and three months would be appropriate. Id.

2. Respondent's Expert, Dr. Christopher A. Mecoli[24]

a. Background and Qualifications

Dr. Mecoli is board certified in internal medicine and rheumatology. Resp. Ex. A at 1; Tr. 101. He received his M.D. from Rutgers University Medical School. Resp. Ex. B at 1. Thereafter, he completed an internal medicine residency at the University of Pennsylvania and a

[23] Immunosenescence is the "decline in immunocompetence with advancing age, characterized by increased susceptibility to infection and tumor formation, decreased response to vaccination, and an increase in autoantibodies and monoclonal immunoglobulins." Immunosenescence, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24933 (last visited July 17, 2024).

[24] Dr. Mecoli submitted two expert reports and testified at the hearing. Resp. Exs. A, C; Tr. 3.

rheumatology fellowship at the Johns Hopkins Hospital. Id.; Tr. 101. During his fellowship he also completed a master's degree in clinical epidemiology and biostatistics. Resp. Ex. B at 1; Tr. 101. Dr. Mecoli currently works at the Johns Hopkins University School of Medicine where he serves as an assistant professor in medicine (mainly rheumatology) and as the director of research operations. Tr. 101-02. In his clinical practice, he regularly evaluates and treats patients with PMR and related conditions. Resp. Ex. A at 1; Tr. 103-04. He has conducted research on rheumatic diseases, particularly myositis and scleroderma, and the underlying triggers of those conditions. Tr. 102. Dr. Mecoli has authored or co-authored numerous publications in the general topic of rheumatology. Tr. 103; Resp. Ex. B at 1-4.

b. Opinion

Dr. Mecoli agreed that Petitioner's appropriate diagnosis was PMR. Tr. 105. However, he disagreed that Petitioner's expert presented a reliable medical theory to explain how the flu vaccine can cause, or did cause, Petitioner's PMR. Id.

He described PMR as a "systemic autoimmune condition," that "impacts the entire body," and generally affects those over age 50, and usually those over 70. Tr. 106. PMR presents with symmetrical discomfort in the shoulders and hips, worse in the morning, and associated with elevated inflammatory markers such as ESR and CRP. Tr. 105-06. Patients usually have a "very robust improvement" to prednisone. Tr. 107. He agreed that genetics may contribute to the incidence of the condition. Tr. 108.

According to Dr. Mecoli, diagnosis is based on history and clinical examination, as well as elevated ESR and CRP. Tr. 108. PMR is treated with prednisone and adjunctive medications like Plaquenil or Methotrexate to reduce the toxicity of prednisone. Tr. 108-09.

i. Althen Prong One

Dr. Mecoli opined that Dr. Efthimiou failed to provide sufficient "evidence and detail" to support a conclusion that there is a causal relationship between the flu vaccine and PMR. Tr. 105. He also noted that Petitioner relied on case reports which he found inadequate to prove a causal association. Resp. Ex. C at 2.

Dr. Mecoli explained that in molecular mimicry there is a "theoretical cross-reactivity." Tr. 126. But as it relates to the flu vaccine and PMR, the theoretical protein sequence in the vaccine that cross-reacts with human protein is not known. Tr. 127-28. In other words, what the immune system is targeting is not known. Id. For example, it is not known whether the theoretical antigen that causes the disease targets muscle cells or synovium. Id. Thus, the "target antigen of the body" is unknown. Tr. 128. Similarly, "the environmental antigen" causing the cross reaction is not known. Id.

As for Petitioner's theory based on cytokine triggered inflammation, Dr. Mecoli did not agree that it reliably explained how the flu vaccine can cause PMR. Tr. 128. Vaccines are intended to trigger an inflammatory response. Id. And Dr. Mecoli stated that the fact that vaccines can trigger inflammation is not evidence of causation. Tr. 129. Dr. Mecoli explained

that elevated inflammatory markers (ESR and CRP) are present in many conditions, and they are "nonspecific finding[s]" that do not prove causation. Id.

Dr. Mecoli noted that both innate and adaptive immune system abnormalities have been observed in PMR. Resp. Ex. A at 6. But "there is no cogent narrative of how exactly the immune system goes awry to result in the clinical features of PMR." Id. He observed that this lack of knowledge is "highlighted" in the medical literature. Id. Dr. Mecoli offered the following quote as an example: "At present, we do not have a clear understanding of the aetiology and pathogenesis of PMR." Id. (quoting Resp. Ex. A3 at 2).[25]

Although Dr. Mecoli disagreed that Petitioner had set forth a reliable mechanism of causation, he agreed with Dr. Efthimiou that there is "likely a genetic predisposition" and "some breakdown of immune tolerance" contributing to the development of PMR. Tr. 117. He also explained that a number of causes have been suggested including infections, cancer, and drugs, "but nothing has really been proven" to cause PMR. Id. He suggested this is because PMR as an illness has received insufficient attention and funding since it does not increase mortality like some other rheumatic conditions do. Id.

As for the implication that the high dose flu vaccine somehow contributed to Petitioner's illness, Dr. Mecoli disagreed. Tr. 119. He testified that it is appropriate to give a high dose to a person of Petitioner's age to illicit an immune response. Id. He also explained that while the high dose flu vaccine at issue here did contain an increase amount of antigen, it did not have an adjuvant. Id.

Regarding Petitioner's reliance on case reports, Dr. Mecoli opined that they are "really low level evidence" of causation, and more "vigorous" studies are needed to assess causality. Tr. 114. In comparison to case reports, he referenced the Nakafero et al.[26] study, which examined 15,000 patients with autoimmune rheumatic illnesses, but not specifically PMR. Tr. 121-23 (citing Resp. Ex. A10). The study did not find a risk of flares associated with the flu vaccination. Id. (citing Resp. Ex. A10).

ii. Althen Prongs Two and Three

Dr. Mecoli opined that the flu vaccine did not cause or contribute to Petitioner's PMR. Tr. 130. He opined that Petitioner had a "very classic presentation" of PMR, with elevated inflammatory markers (ESR and CRP), and she responded well to low to moderate doses of prednisone. Tr. 109. She did not have any signs or symptoms of GCA, which some patients with PMR may have. Tr. 111.

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[25] Dario Camellino et al., Pathogenesis, Diagnosis and Management of Polymyalgia Rheumatica, 36 Drugs & Aging 1015 (2019).

[26] Georgina Nakafero et al., Association Between Inactivated Influenza Vaccine and Primary Care Consultations for Autoimmune Rheumatic Disease Flares: A Self-Controlled Case Series Study Using Data From The Clinical Practice Research Datalink, 78 Annals Rheumatic Diseases 1122 (2019).

While Dr. Mecoli agreed that there was "a temporal association between the vaccine and the onset of [Petitioner's] PMR symptoms," he did not agree that a temporal association proved causation. Tr. 113. Further, he did not agree that onset of one week after vaccination supported a mechanism of cytokine induced inflammation. Resp. Ex. A at 6. For example, he opined that the cytokine IL-6 "rises in the first 24-48 hours" after vaccination and "correlates with symptoms." Id. According to Dr. Mecoli, the fact that Petitioner's symptoms did not begin until approximately one week after vaccination, weakens her reliance on a cytokine theory of causation. Id.

IV. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, Petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157,

162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Causation

To receive compensation through the Program, a petitioner must prove either (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioner does not allege she suffered a Table Injury, she must prove a vaccine she received caused her injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d. 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether a petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The

Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

V. CAUSATION ANALYSIS

A. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds Petitioner has failed to provide preponderant evidence of a sound and reliable theory to explain how the flu vaccination can cause PMR. There are several reasons for this finding.

First, and most importantly, Petitioner's expert offered very cursory statements about causal mechanisms without explanation, context, or foundational support. In his expert reports, Dr. Efthimiou simply stated there was "aberrant activation" and "broad non-specific overactivation" of the immune system. Pet. Ex. 17 at 3; Pet. Ex. 22 at 2. He offered no explanation about what these phrases meant. And he did not explain how the flu vaccine caused aberrant activation, or how aberrant activation caused PMR. While the medical literature may include the same phrase, "aberrant activation of the immune system," to generally describe the cause of PMR, it is too broad and too vague when used to prove vaccine causation by the preponderant of evidence standard. See Resp. Ex. A2 at 5.[27]

[27] G. Guggino et al., Pathogenesis of Polymyalgia Rheumatica, 70 Reumatismo 10 (2018).

At the hearing, Dr. Efthimiou offered two theories: molecular mimicry and cytokine-induced inflammation. But he offered very little explanation and did not develop either of these ideas by providing basic foundational evidence to explain how the flu vaccine could cause PMR. In response, Dr. Mecoli asked basic relevant questions. For molecular mimicry, he asked, what is thought to be the antigen in the vaccine that triggers cross-reactivity? What is the target of the cross-reactivity in the body? And how does that cause PMR? Overall, Dr. Mecoli's opinions were much more persuasive, especially since he cited medical literature in support of the fundamental opinions that he offered.

Simply asserting a causal theory without context or a supportive factual framework based on medical literature, research, or other evidence is insufficient. The causal theory must be specific to the petitioner's case. Moberly, 592 F.3d at 1322. Merely identifying a mechanism for a disease process without additional evidence specific to Petitioner's case is insufficient to preponderantly show causation. See Monzon v. Sec'y of Health & Hum. Servs., No. 17-1055V, 2021 WL 2711289, at *29 (Fed. Cl. Spec. Mstr. June 2, 2021); Baron v. Sec'y of Health & Hum. Servs., No. 14-341V, 2019 WL 2273484, at *17 (Fed. Cl. Spec. Mstr. Mar. 18, 2019); Duncan v. Sec'y of Health & Hum. Servs., No. 16-1367V, 2020 WL 6738228, at *11 (Fed. Cl. Spec. Mstr. Oct. 19, 2020), aff'd, 153 Fed. Cl. 642 (2021); Boatmon, 941 F.3d at 1360; LaLonde v. Sec'y of Health & Hum. Servs., 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing Moberly, 592 F.3d at 1322); W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352, 1356 (Fed. Cir. 2013).

Although molecular mimicry is an accepted scientific mechanism, generally opining that molecular mimicry is a causal theory, without more, is insufficient. See, e.g., W.C., 704 F.3d at 1360 (noting "[t]he special master found that molecular mimicry is a well-regarded theory in some contexts, but correctly required additional evidence showing that molecular mimicry can cause the [flu] vaccine to significantly aggravate [the alleged injury]" (internal citations and quotations omitted) (citing Broekelschen, 618 F.3d at 1345)); Loyd ex rel. C.L. v. Sec'y of Health & Hum. Servs., No. 16-811V, 2021 WL 2708941, at *31 (Fed. Cl. Spec. Mstr. May 20, 2021) ("[T]hough molecular mimicry is a generally accepted scientific concept, and is frequently invoked in Program cases, the mere mention of it does not constitute satisfaction of the preponderant evidentiary standard. Rather, it must be shown that the mechanism likely does link the vaccine in question to the relevant injury." (internal citations omitted)); McKown v. Sec'y of Health & Hum. Servs., No. 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019) (explaining that "merely chanting the magic words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent additional evidence specifically tying the mechanism to the injury and/or vaccine in question" (emphasis omitted)); Johnson v. Sec'y of Health & Hum. Servs., No. 14-254V, 2018 WL 2051760, at *26 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) ("Petitioners cannot simply invoke the concept of molecular mimicry and call it a day. Rather, they need to offer reliable and persuasive medical or scientific evidence of some kind (whether expert testimony or literature) . . . ." (internal citations omitted) (emphasis omitted)); Mattus-Long v. Sec'y of Health & Hum. Servs., No. 15-113V, 2022 WL 4242140, at *27 (Fed. Cl. Spec. Mstr. Aug. 31, 2022) (noting "the mere mention of molecular mimicry is not a 'get out of jail free card' in the Program, entitling claimants to compensation, merely because it has scientific reliability as a general matter"); Sheets v. Sec'y of Health & Hum. Servs., No. 16-1173V, 2019 WL 2296212, at *17 (Fed. Cl. Spec. Mstr. Apr. 30, 2019) (determining the

petitioner had not satisfied Althen prong one when he did not relate molecular mimicry "to either the vaccines in question or [p]etitioner's own specific condition").

Next, while the undersigned generally finds case studies may provide some evidence of causation, Petitioner's cited case reports here do not provide support for finding causation. The case report by Iwata and Mizuno relates to a patient who had an infection, not a vaccination. And Dr. Efthimiou did not explain how an infectious cause could be attributed to a vaccine. The PMR patient described by Bassednine and Bridge received an adjuvanted vaccination. The vaccine at issue here did not contain an adjuvant. And the Soriano et al. and Wada et al. papers discuss patients with combined PMR and GCA. The relevance of these articles is not clear, especially since Petitioner's expert did not opine that GCA involved the same causal mechanism as PMR. "An expert may 'extrapolate from existing data,' and use 'circumstantial evidence,' [b]ut the reasons for the extrapolation should be transparent and persuasive." K.O. v. Sec'y of Health & Hum. Servs., No. 13-472V, 2016 WL 7634491, at *12 (Fed. Cl. Spec. Mstr. July 7, 2016) (internal citations omitted) (first quoting Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 743 (2009); and then quoting Althen, 418 F.3d at 1280).

Petitioner need not make a specific type of evidentiary showing or require identification of a specific antigenic trigger for an immune-mediated pathology to prove that a theory is sound and reliable by preponderant evidence. Given the state of current scientific knowledge as it relates to PMR, there is no way that a petitioner could satisfy such a requirement, especially here where neither of the experts could identify any cross-reacting proteins based on the current state of available knowledge. Further, requiring proof of the identify of a specific antigen to prove causation would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program").

Here, there is a basic lack of knowledge well-documented in the medical literature. Pet. Ex. 18 at 1 (noting "the etiology of PMR remains unknown"); Pet. Ex. 19 at 1 ("The etiology and pathogenesis of PMR remains obscure."); Pet. Ex. 29 at 1 ("The aetiology is not fully understood, but there are associated environmental and genetic factors."); Resp. Ex. A2 at 1 (PMR "is a chronic, inflammatory disorder of unknown cause."); Resp. Ex. A3 at 2 ("At present, we do not have a clear understanding of the aetiology and pathogenesis of PMR."). However, a void of knowledge about the pathogenesis of disease cannot be filled by non-specific and vague statements or supposition.

Finally, there are three other Program cases with reasoned analyses regarding vaccine causation and PMR, and entitlement has been denied.[28] Van Dycke v. Sec'y of Health & Hum. Servs., No. 18-106V, 2023 WL 4310701 (Fed. Cl. Spec. Mstr. June 7, 2023); Suliman v. Sec'y of Health & Hum. Servs., No. 13-993V, 2018 WL 6803697 (Fed. Cl. Spec. Mstr. Nov. 27, 2018); Kelly v. Sec'y of Health & Hum. Servs., No. 17-1475V, 2022 WL 17819157 (Fed. Cl.

[28] In a fourth case, diagnosis was at issue and the special master found that preponderant evidence did not show that the petitioner had the injury alleged (PMR). Giesbrecht v. Sec'y of Health & Hum. Servs., No. 16-1338V, 2023 WL 2721578, at *5-7 (Fed. Cl. Spec. Mstr. Mar. 30, 2023).

Spec. Mstr. Oct. 12, 2022). While the mechanisms may differ, PMR has been rejected as a vaccine-related injury. Although decisions of other special masters are not binding, the undersigned generally agrees with the reasoning of her colleagues in these cases. See Boatmon, 941 F.3d at 1358; Hanlon v. Sec'y of Health & Hum. Servs., 40 Fed. Cl. 625, 630 (1998), aff'd, 191 F.3d 1344 (Fed. Cir. 1999).

In Van Dycke, the petitioner alleged that he suffered PMR and GCA due to a tetanus-diphtheria-acellular pertussis ("Tdap") vaccination. Van Dycke, 2023 WL 4310701, at *1. The theory offered involved T-cell activation but was not antigen specific and did not involve molecular mimicry. Id. at *22. Instead, it involved the formation of a neoantigen present due to senescence. Id. The undersigned found the theory was unsupported by medical evidence, research, or other reliable evidence. Id. at *22-27.

In Suliman, the petitioner alleged she suffered PMR and/or myositis as a result of the Tdap vaccine. Suliman, 2018 WL 6803697, at *25-27. Petitioner's expert offered the autoimmune syndrome induced by adjuvants ("ASIA") theory. Id. The special master determined petitioner's expert did not effectively explain how the aluminum adjuvant in the Tdap vaccine could cause PMR and/or myositis. Id.

In Kelly, the petitioner alleged she suffered PMR as a result of the flu vaccine. Kelly, 2022 WL 17819157, at *1. Like here, petitioner's expert offered molecular mimicry as the theory of causation. Id. at *6. The special master found petitioner's expert was not persuasive in identifying "components of the flu vaccine that could be mimicked to cause PMR or in alternatively invoking GCA to circumstantially identify a mechanism of cell-mediated autoimmunity.") Id.; see also C.P. v. Sec'y of Health & Hum. Servs., No. 14-917V, 2019 WL 5483621, at *26, *28 (Fed. Cl. Spec. Mstr. Aug. 21, 2019) (denying entitlement where the theory was molecular mimicry and there was no evidence of homology).

Overall, the undersigned finds that Petitioner's theories of aberrant or overactive immune system response, molecular mimicry, and cytokine driven inflammation are too nonspecific and lack foundational support from medical articles, scientific facts, research, or any other reliable evidence. As such, the theories are conclusory in nature. When evaluating whether petitioners have carried their burden of proof, special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *31 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, decision aff'd, 141 Fed. Cl. 138, aff'd, 945 F.3d 1362 (Fed. Cir. 2020). The undersigned will not rely on "opinion evidence that is connected to existing data only by the ipse dixit of the expert." Prokopeas v. Sec'y of Health & Hum. Servs., No. 04-1717V, 2019 WL 2509626, at *19 (Fed. Cl. Spec. Mstr. May 24, 2019) (quoting Moberly, 592 F.3d at 1315). Instead, special masters are expected to carefully scrutinize the reliability of each expert report submitted. See id.

In summary, Petitioner has failed to offer a sound and reliable medical theory in support of her claim. Thus, the undersigned finds Petitioner has failed to provide preponderant evidence with respect to the first Althen prong.

B. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (fed. Cir. 1993). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since Petitioner failed to prove Althen prong one, it follows that she cannot prove Althen prong two. However, even if Petitioner had proven Althen prong one, the undersigned finds Petitioner has failed to show by preponderant evidence that there is a logical sequence of cause and effect showing Petitioner's flu vaccine caused her PMR.

The undersigned finds that two of Petitioner's treating physicians documented her reports of symptoms and/or their temporal association with her flu vaccination, but they did not opine that her vaccination caused her PMR.

Treating physician statements are typically "favored" since they "are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" Capizzano, 440 F.3d at 1326 (quoting Althen, 418 F.3d at 1280). However, no treating physician's views bind the special master, per se; rather, their views are carefully considered and evaluated. § 13(b)(1); Snyder, 88 Fed. Cl. at 746 n.67. "As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases." Welch v. Sec'y of Health & Hum. Servs., No. 18-494V, 2019 WL 3494360, at *8 (Fed. Cl. Spec. Mstr. July 2, 2019).

Petitioner reported to her PCP, Dr. Cathcart, that her hip pain began about one week after receiving the flu vaccination. Rheumatologist Dr. Keroack also noted in the documented history that Petitioner's myalgias in her thighs and shoulders started about a week after the flu

vaccination. Neither physician, however, documented any opinion causally associating Petitioner's PMR to her flu vaccination.[29]

Therefore, the undersigned finds that the above entries in the medical records do not provide evidence of causation. This position is consistent with case law. "A treating physician's recognition of a temporal relationship does not advance the analysis of causation." Isaac v. Sec'y of Health & Hum. Servs., No. 08-601V, 2012 WL 3609993, at *26 (Fed. Cl. Spec. Mstr. July 30, 2012); see also A.T. v. Sec'y of Health & Hum. Servs., No. 16-393V, 2021 WL 6495241, at *28 (Fed. Cl. Spec. Mstr. Dec. 17, 2021) (finding that petitioner's treating physicians "considered, though did not conclude," that petitioner's vaccine significantly aggravated her condition); Robertson v. Sec'y of Health & Hum. Servs., No. 18-554V, 2022 WL 17484980, at *17 (Fed. Cl. Spec. Mstr. Dec. 7, 2022) (finding treating physicians' statements of mere suspicion fall short of an opinion supporting vaccine causation); Cedillo v. Sec'y of Health & Hum. Servs., 617 F.3d 1328, 1347 (Fed. Cir. 2010) (concluding the special master did not err in affording little weight to the opinions of petitioner's treating physicians where "none of the treating physicians concluded that the [] vaccine caused [petitioner's] [condition]").

Accordingly, the undersigned finds that Petitioner failed to satisfy her burden under Althen prong two.

C. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been defined as a "medically acceptable temporal relationship." Id. The Petitioner must offer "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542; see also Pafford, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., Veryzer, 100 Fed. Cl. at 356 (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that [P]etitioner must posit a medical theory causally connecting the vaccine and injury").

Petitioner received the flu vaccination at issue on December 1, 2015, and the medical records document that she reported the onset of hip pain began about one week after she received

[29] In her pre-hearing submission, Petitioner stated she consulted with Dr. Dichiaro, "who opined that [Petitioner] should continue to avoid flu vaccinations in the future due to what appears to have been an adverse reaction to the same." Pet. Updated Pre-Hearing Submission at 2 (citing Pet. Exs 1-2.). The undersigned did not find any records by Dr. Dichiaro advising that Petitioner should avoid flu vaccinations in the future due to any past adverse reaction. Even assuming, however, that such a record did exist, it would not change the outcome here for all of the reasons explained herein.

her vaccination. Petitioner reported the same history about the onset of her hip pain to two different providers, Dr. Cathcart and Dr. Keroack. The undersigned finds the records of these two providers are the most contemporaneous and reliable evidence of the onset of Petitioner's PMR. Moreover, Respondent's expert agrees that onset occurred about one week after vaccination. Based upon all of the evidence, the undersigned finds that the onset of Petitioner's PMR was about one week after vaccination.

Respondent does not contest that there is a temporal association between Petitioner's flu vaccination and the onset of her PMR. See Tr. 113. However, Respondent disagrees that the onset of one week would be appropriate given the theory based on cytokine induced inflammation. See Resp. Ex. A at 6. The undersigned agrees.

Respondent's expert did not opine that an onset of one week would be inappropriate if the theory of causation was molecular mimicry. Thus, Petitioner has provided preponderant evidence satisfying Althen prong three only as to molecular mimicry. However, a temporal association, without more, is insufficient. Moberly, 592 F.3d at 1323; Grant v. Sec'y of Health & Hum. Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("[A] proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury."). Thus, Petitioner is not entitled to compensation.

VI. CONCLUSION

The undersigned extends her sympathy to Petitioner for the pain and suffering that she experienced due to her illness. The undersigned's Decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

For the reasons discussed above, the undersigned finds that Petitioner has failed to establish by preponderant evidence that her flu vaccination caused her PMR. Therefore, Petitioner is not entitled to compensation and the petition must be dismissed.

In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master